REMARKS

In the claims

Claims 4, 13, 16, 21, 22, and 24 are pending with claims 1–3, 5–12, 14, 15, 17–20, 23 and 25–29 cancelled without prejudice or disclaimer. Claims 30–38 are added by this paper.

Claim amendments

Claim 4 recites additional Group I aspects of Applicants' invention and is supported by the disclosure contained throughout the specification, as originally filed. For example, see, the paragraph bridging pages 6 and 7; page 8, lines 28–35; and the disclosure contained in Example 1. Support for the kit claims and the claims dependent therefrom can be found at page 12, lines 15–31 and at least by the Examples.

The subject matter of now cancelled claim 1 is incorporated into the kit claim of claim 24.

The amendments do not raise new matter.

Restriction/election

Claims 16, which is dependent on examined claim 4, stands improperly restricted. Despite Applicants' request for the reinstatement of these improperly restricted claims, the Patent Office has maintained the requirement with the contention that it would be undue burden to search and/or examine the claims. Applicants courteously disagree with this reasoning.

Claim 16 is drawn to a combination (an agent of claim 4 and, e.g., an excipient) which requires the particulars of the subcombination (claim 4). "Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations." See, MPEP § 806.05(c). In the absence of such a showing, the Office is courteously requested to reinstate claim 16.

The Office is therefore courteously requested to reinstate the withdrawn claim.

Specification

Applicants prefer not to use the PTO's suggested subtitles since these are not mandatory.

Rejections under 35 U.S.C. §112, second paragraph

The rejections, not specifically discussed herein, are moot in view of the amendments. Withdrawal of the rejection is courteously requested.

Rejections under 35 U.S.C. §112, first paragraph

The Office Action alleges that the specification does not provide a written description of the claimed subject matter and fails to comply with the enablement requirement. As such, the claims of the instant application stand rejected under 35 U.S.C. §112, first paragraph. Applicants courteously traverse this rejection.

At page 7, the Office Action alleges that "the specification contains no working examples to substantiate the assertion [that overexpression of PRV-1 on granulocytes contributes to hyperproliferation of granulocytes], and the art does not support this conclusion." The Office Action then uses Pahl's disclosure (*Eur. J. Biochem.*, **vol. 267**, pages 3395–3401, **2000**) to corroborate this contention. Applicants courteously disagree with this analysis.

The specification provides adequate guidance on the cellular effects of PRV-1 signaling. See, for example, page 5, lines 26–32 of the specification. More specifically, it is expressly disclosed that the over-expression of PRV-1 gene in the granulocyte of p. vera patients contributes to the hyperproliferation of such cells. Moreover, Example 3 of the Applicants' specification provides experimental evidence to growth factor-like effects of PRV-1. For example, treatment with PRV-1-containing medium resulted in the formation of many more haematopoietic colonies [i.e., erythroid colony-forming units (CFU-Es)] than did

control cells. These results scientifically corroborate with Applicants' disclosure that PRV-1 mediated transduction of mitogenic signals plays a role in cell proliferation. In view of the detailed disclosure contained in the specification and the body of relevant prior art knowledge on PRV-1 proteins, the Office's allegation that "the specification contains no working examples to substantiate [the claimed subject matter]" is completely misplaced.

It is courteously submitted that the Office Action provides a severely lopsided analysis of Pahl's disclosure. The Examiner while quoting Pahl, has chosen to ignore the very concluding sentence of the quoted paragraph, wherein it is stated, "It is therefore likely that PRV-1 also mediates signal transduction in bone marrow cells." (Emphasis added) Additionally, the role of PRV-1 in the hematopoetic differentiation pathway, particularly in the case of granulocytes, is further corroborated by numerous art references, including the findings of Temerinac et al. (Blood, **vol. 95**, pages: 2569-2576, **2000**), which is relied upon by the Examiner.

Applicants also courteously disagree with the Office's contention that the claimed use of the PRV-1 polypeptides as a diagnostic marker is not enabled by the specification. For example, page 8 of the open Office Action uses Klippel et al.'s disclosure to support this contention. However, Applicants respectfully submit that in view of the subsequent disclosures by Klippel and others, expression profiling of PRV-1 and its gene products is both a scientifically-accepted as well as a routinely-used technique for the detection of PV in clinical isolates. See, for example Klippel et al. (Blood, **vol. 102**, pages: 3569-3574, **2003**) and the subsequent confirmatory report by Cillioni et al. (Blood, **vol. 103**, pages: 2428-2429, **2004**). The Office is courteously requested to review the enclosed article by Klippel (2003), wherein in the ABSTRACT Kippel expressly states that:

> PV patients express significantly higher amounts of PRV-1 than healthy controls or patients with SE ($P < .0001$). Because there is no overlap between the PRV-1 expression in PV patients versus healthy controls or SE patients, the assay has a very high sensitivity and specificity for the diagnosis of PV in our population. (Emphasis added)
>
> -Klippel et al., *Blood*, **vol. 102**, pages: 3569-3574, **2003**.

Based on the disclosure contained in the specification and the operative

embodiments contained in the Examples, one of ordinary skill in the art could routinely screen for the claimed malignancies by analyzing the expression and/or levels of PRV-1 gene or its product(s) in any relevant biological specimen (for example, blood, tissues, or biopsy samples). Such would be totally commensurate with what is claimed by the instant invention.

Applicants courteously submit that to maintain the rejection under these circumstances would not only be contrary to the Patent Office's own published standards, but also be blind to the overwhelming scientific evidence regarding the utility of the claimed polypeptides. Accordingly, it is requested that the pending rejection be withdrawn.

Rejection under 35 U.S.C. §112, first paragraph (enablement)

The specification coupled with a skilled worker's knowledge provides adequate guidance to make and use the claimed libraries. The specification provides both general and specific guidance regarding the structural features and utility of the claimed compounds. In the absence of evidence which demonstrates otherwise, all claims must be taken to satisfy the requirements of 35 U.S.C. § 112, first paragraph. Moreover, only one use needs to be enabled for compound claims. Here, the focus is on PRV-1 mediated cell proliferation. See, Example 3 at pages 16–17 of the instant specification.

Contrary to the Examiner's assertion, the specification provides detailed guidance on "how to use" the polypeptides of the instant invention for the claimed methods. For example, techniques for assessing PRV-1 gene expression and/or measuring the levels of PRV-1 protein are provided at page 9–11 of the specification; hematological malignancies that are treatable using the polypeptides of the instant invention, including methods for treating such malignancies are provided at page 12 of the specification; Example 3 demonstrates that treatment of cells with PRV-1 protein led to increased proliferation (i.e., colony formation). The preceding example (Example 2) at page 14 of instant application provides experimental details for the isolation and purification of the claimed proteins. Example 4 imparts a clinical utility to the aforementioned observation by providing a working example of the detection of PRV-1 protein in a clinical isolate.

In view of the above remarks, it is respectfully submitted that Applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention with an effort that is routine within the art. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph is respectfully requested.

Rejection under 35 U.S.C. §102(b)

Claims 1–3, and 12 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Temerinac's scientific disclosures, the earliest of which pertains to the publication in *Leukemia Research*, **vol. 23**, supplement 1, **1999**. This rejection is respectfully traversed.

It is respectfully submitted that upon the Examiner's verification of Applicants' claim to priority, in view of the verified translation of the priority document (DE 198 49 044.5), the above-mentioned rejection will be rendered moot. Withdrawal of the rejection is respectfully requested.

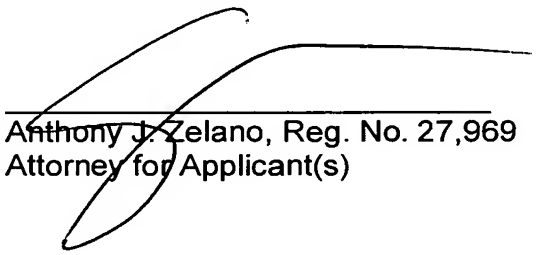
Double patenting rejections

Claim 4 of this application has been rejected under the doctrine of obviousness-type double patenting over all claims of US Patent No. 6,686,153. Applicants respectfully disagree that the claims of a given application render obvious the claims of the other application. However, in order to expedite prosecution, a terminal disclaimer as to this patent application is being provided herewith. Thus, it is submitted that the rejection is moot in view of the terminal disclaimer. Withdrawal of the rejection is courteously requested.

In view of the above-mentioned arguments and amendments, it is respectfully submitted that the claims in the application are in condition for allowance. However, if the Examiner has any questions or comments, he is cordially invited to telephone the undersigned at the number below.

Enclosed is a check of $225.00 for the two-month extension-of-time fees (small entity). No fees are believed to be due with this response; however, the Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,



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